

Figure 1

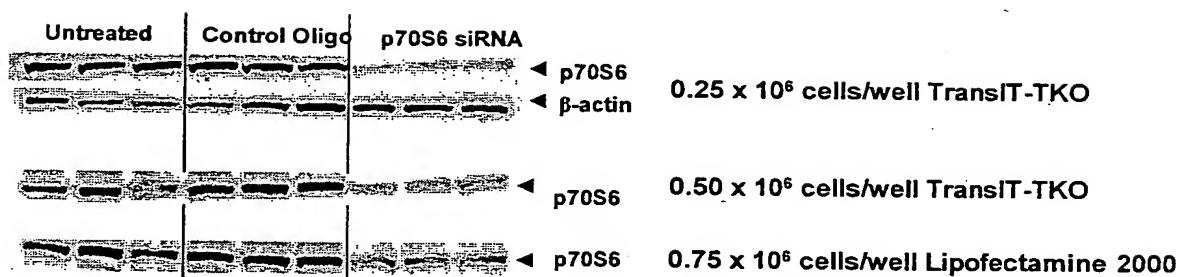


Figure 2

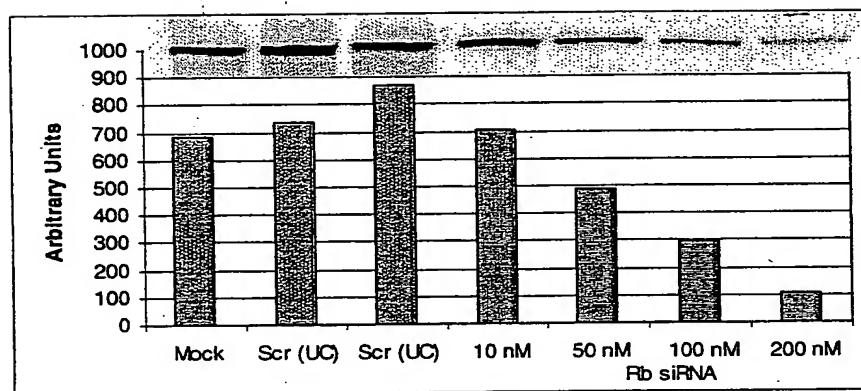


Figure 3

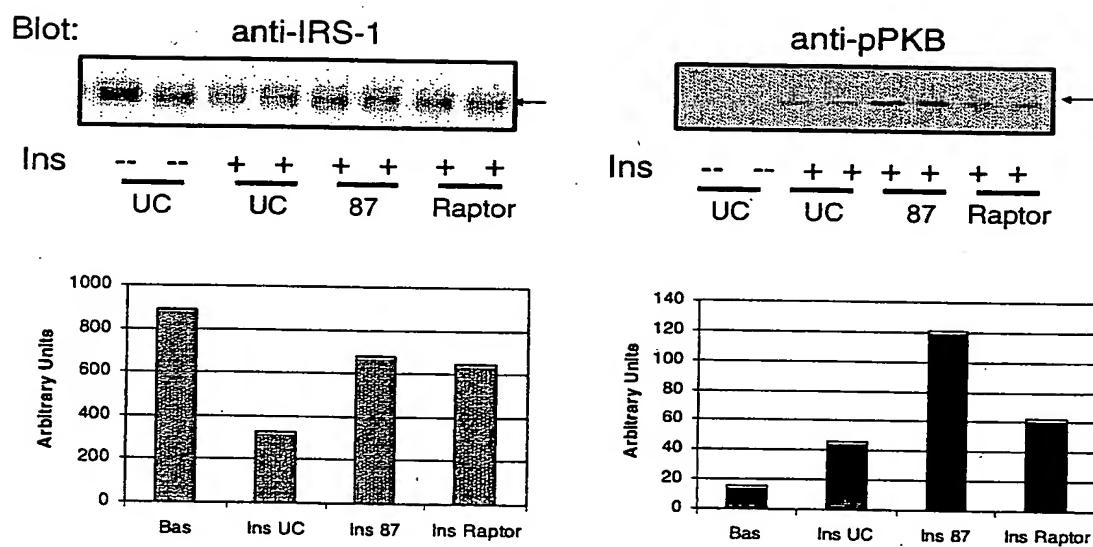


Figure 4

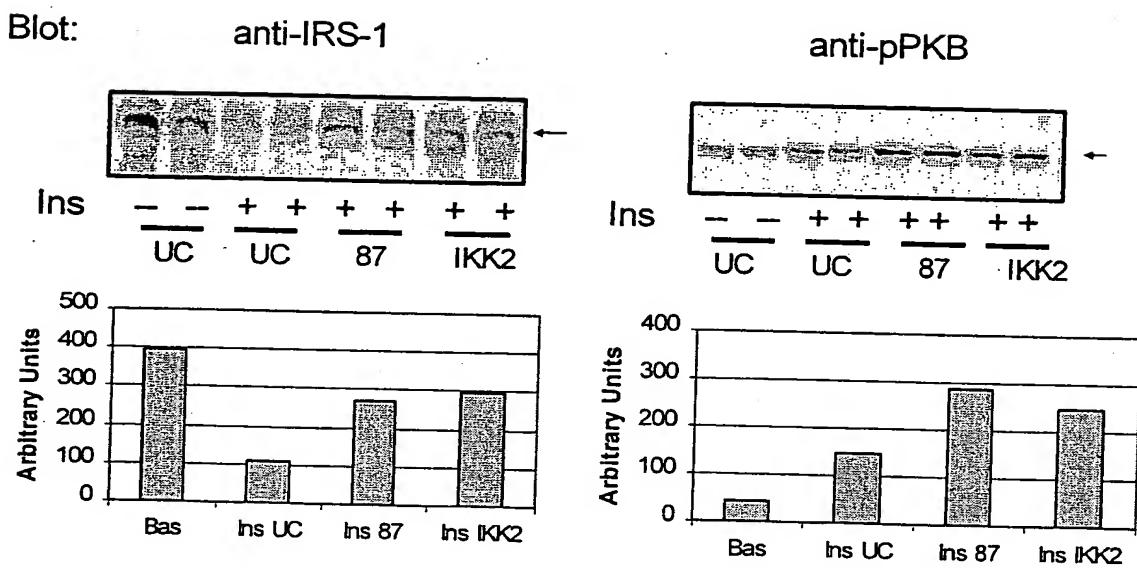


Figure 5

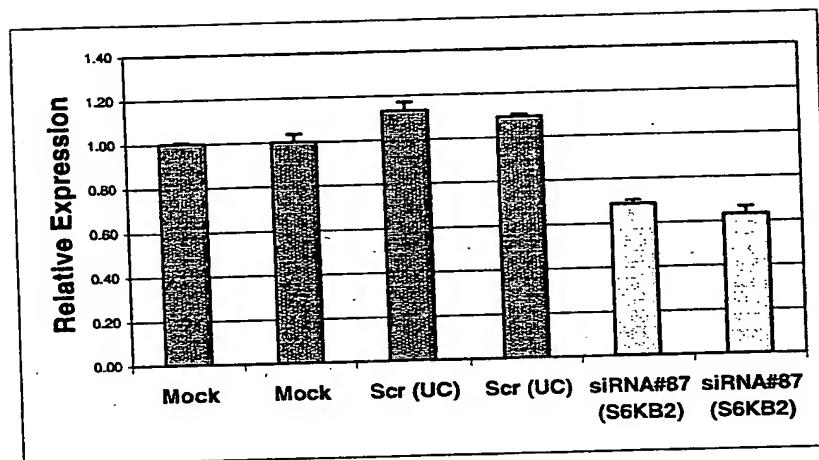
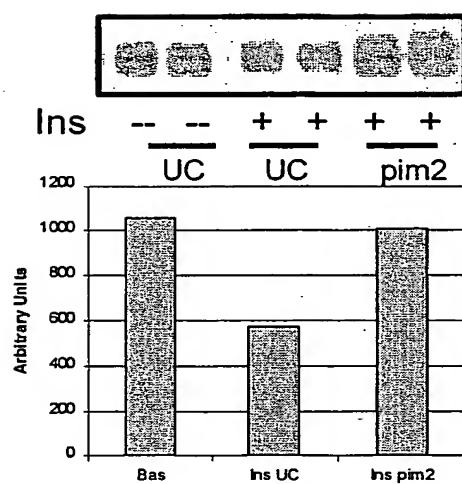


Figure 6

Blot:

anti-HRS-1



anti-pPKB

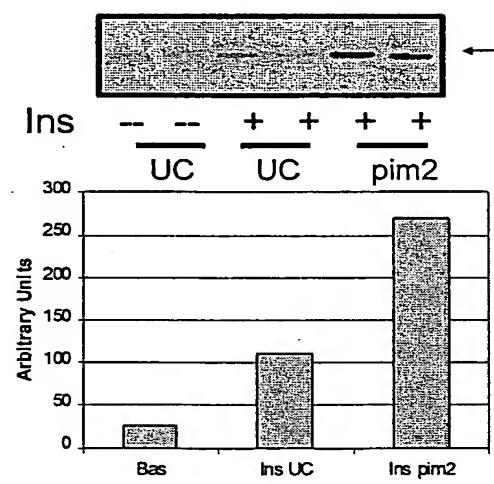


Figure 7

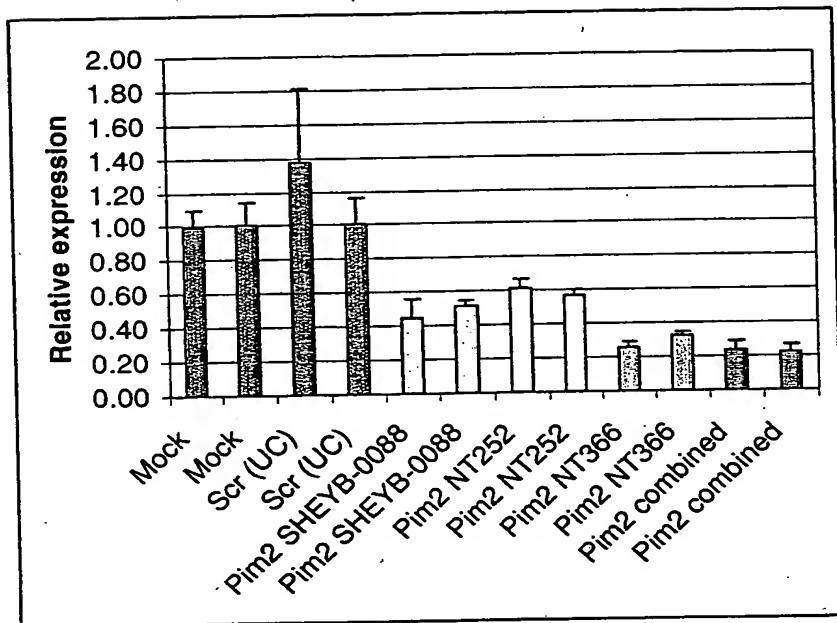
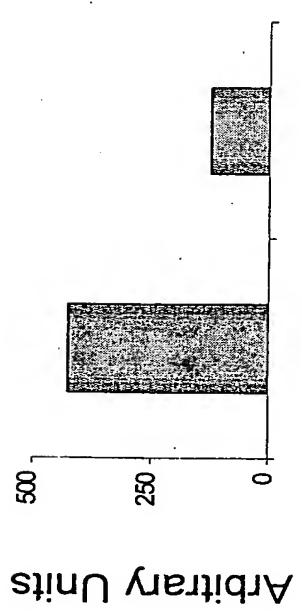


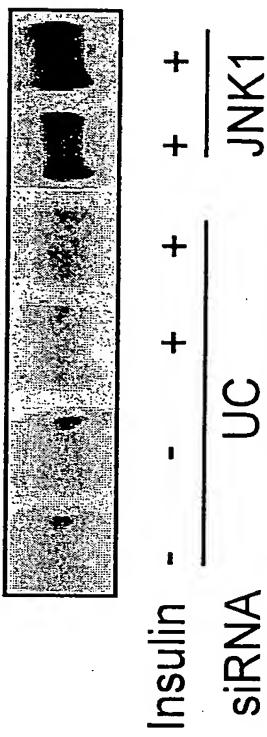
Figure 8

Reduction of JNK-1 inhibits IRS-1 degradation and enhances insulin-induced PKB phosphorylation

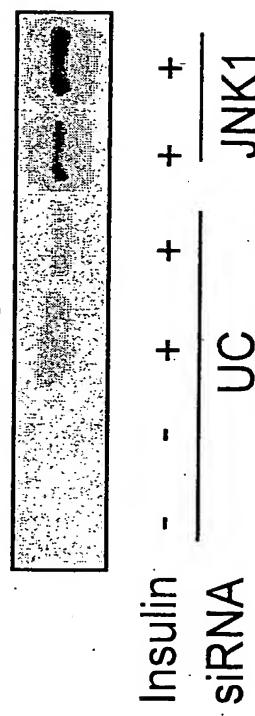
JNK-1 protein expression



Anti-IRS-1



Anti-pPKB

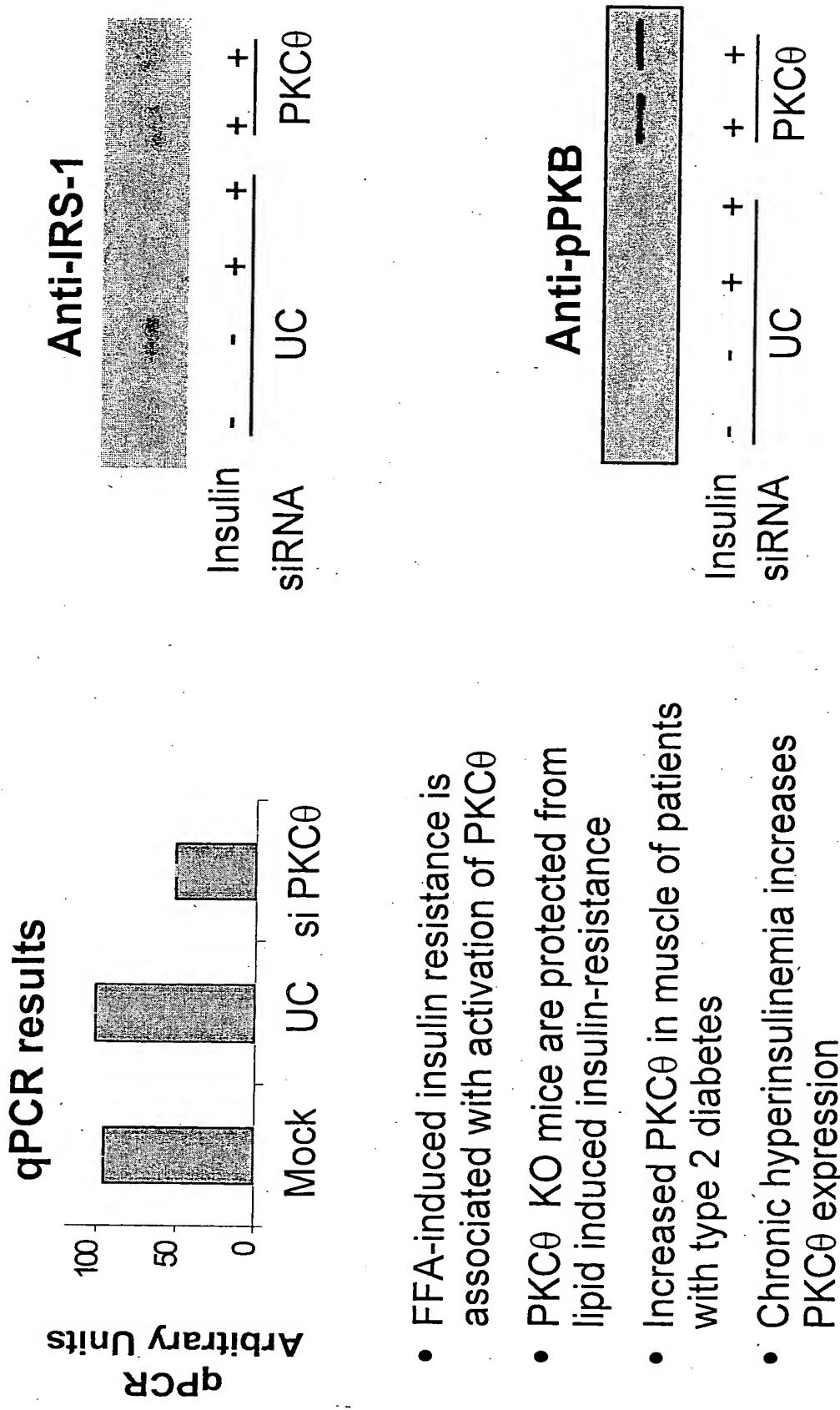


- JNK activity is elevated in Type 2 diabetes and insulin resistance states
- JNK-1 -/- are protected to the development of diet induced obesity and insulin-resistance
- Reduction of JNK-1 in ob/ob mice improves insulin sensitivity and prevents diabetes

Fig. 9

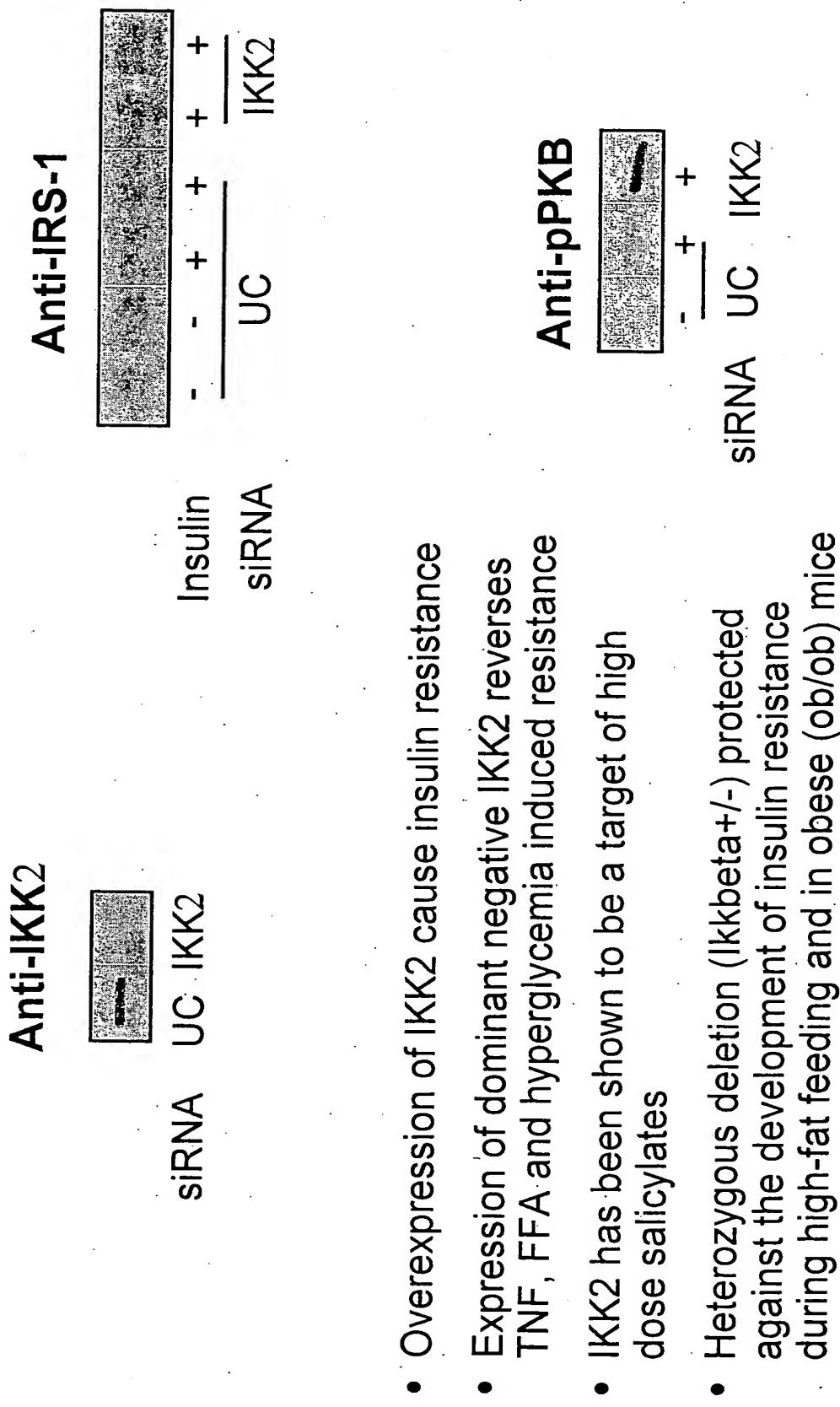
Reduction of PKC θ inhibits IRS-1 degradation and enhances insulin-induced PKB phosphorylation

Fig. 10



Reduction of IKK2 inhibits IRS-1 degradation and enhances insulin-induced PKB phosphorylation

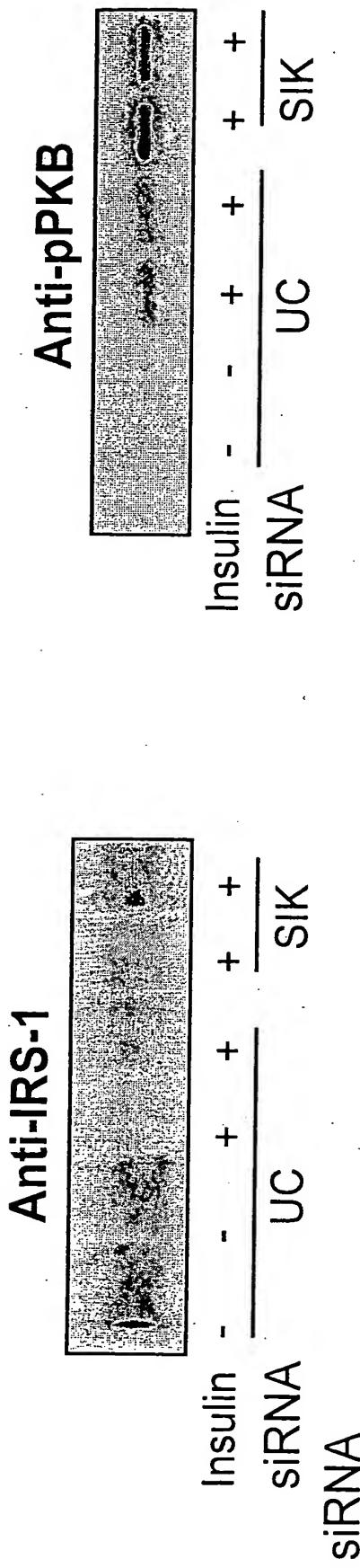
Fig. 11



- Overexpression of IKK2 cause insulin resistance
- Expression of dominant negative IKK2 reverses TNF, FFA and hyperglycemia induced resistance
- IKK2 has been shown to be a target of high dose salicylates
- Heterozygous deletion (*Ikkbeta^{+/−}*) protected against the development of insulin resistance during high-fat feeding and in obese (ob/ob) mice

Salt-inducible kinase-1 (SIK) is a new kinase involved in insulin resistance

Fig. 12



- SIK was first cloned from the adrenal glands of rats fed a high salt diet
- Serine/threonine protein kinase that belongs to AMPK family
- SIK1 mRNA is elevated in adipose tissues, livers, and skeletal muscle of diabetic animals
- Involved in the phosphorylation of Ser⁷⁸⁹ in IRS-1 in livers of diabetic animals